REMARKS

Prior to entry of this Amendment, Claims 1-73 were pending and under consideration. With this Amendment, Claims 7-20 and 36-50 are being cancelled, without prejudice or disclaimer, and Claims 21, 23-24, 26-33, 53-54, 56-59, 62-64, 66-67 and 69-73 are being amended. No claims are being added. Thus, after entry of this Amendment, Claims 1-6, 21-35 and 51-73 are pending and under consideration.

I. Amendments of the Claims

Claims 7-20 and 36-50 have been cancelled, without prejudice against their reintroduction into this or one or more related applications, in order to reduce the issues going forward. In addition, Claims 21, 23-24, 26-33, 53-54, 56-59, 62-64, 66-67 and 69-73 have been amended.

Claim 21 has been amended in both the preamble and body. The preamble has been amended to read "A method of detecting the presence of a predetermined target nucleic acid sequence in a sample." This amendment is supported at, for example, Col. 11, lines 3-6 of the issued patent. The body has been amended to clarify the conditions under which the contacting is carried out and under which the recited probes specifically hybridize to the target sequence. Specifically, Claim 21 now recites that the contacting is carried out under conditions in which a FEN-1 polypeptide exhibits cleavage activity and that it is under such cleavage conditions that the 3'-region of the 5'-probe and the 5'-region of the 3'-probe are capable of specifically hybridizing to their respective portions of the target sequence. These amendments are supported by the text of the original patent at, for example, Col. 11, lines 6-8, 11-13 and 20-24, wherein it is taught that the sample and probes are incubated with a FEN-1 polypeptide and the release of nucleotides or polynucleotides (*i.e.*, cleavage) is detected.

Claim 21 has also been amended to recite that the 5'-probe, 3'-probe and target sequence hybridize with one another to form a 5',3'-double flap structure that is cleavable by a FEN-1 polypeptide. Support for this amendment was discussed in detail in connection with the rejection under 35 U.S.C. § 251 in Applicant's Amendment of August 13, 2003 (Paper No. 26).

Claim 59, although directed to a kit, has been amended in a manner similar to Claim 21. In addition, the preamble of Claim 59 has been amended to recite "a kit for use in ....". The amendments of Claim 59 are supported by the sections pointed out in connection with Claim 21.

Claims 23-24, 53-54 and 66-67 have been amended to clarify the region of the 5'-probe that contains the detectable label.

Claims 26-27 and 69-70 have been amended to recite that the FEN-1 polypeptide is encoded by polynucleotides corresponding in scope with the polynucleotides of Claims 2 and 3, respectively.

Claims 28-30 have been amended to depend from Claim 21 instead of Claim 26 to maintain proper antecedent basis in light of the amendment of Claim 26.

Claims 31-32, 56-57 and 62-63 have been amended to recite the region of the 3'-probe that contains the stated number of nucleotides. Claims 33, 58 and 64 have been amended to recite the region of the 5'-probe that contains the stated number of nucleotides. Support for these amendments was discussed in more detail in connection with the rejection under 35 U.S.C. § 112, ¶ 1 in Applicant's Amendment of August 13, 2003 (Paper No. 26).

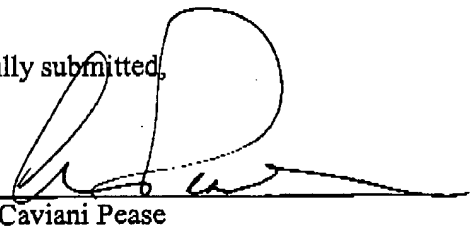
Lastly, Claims 71-73 have been amended for clarity and to multiply depend from Claims 59-68. These amendments were necessitated by the amendment of Claim 69.

For reasons outlined above, or that were discussed in Applicant's Amendment filed August 13, 2003 (Paper No. 26), which are incorporated herein by reference, none of these amendments present new matter under 35 U.S.C. § 251. Entry into the application is therefore requested.

VI. Conclusion

Claims 21-35 and 51-73 are believed to be in condition for allowance. An early indication of the same is therefore kindly requested. No fees beyond those being submitted concurrently with this Amendment are believed due. However the Commissioner is authorized to charge any required fees, or credit any overpayment to Deposit Account No. 50-2319 (Order No. RI-71904).

Respectfully submitted,

Date: 1/24/2004 By: 

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APPENDIX A

Marked-Up Version of Amended Claims Showing Changes

21. (Twice Amended) A method of detecting the presence of a predetermined target nucleic acid sequence in a sample, comprising the steps of:

(a) contacting, under conditions in which a FEN-1 polypeptide exhibits cleavage activity, a sample suspected of containing a target nucleic acid comprising the predetermined target sequence ~~of interest~~ with:

~~(i) a FEN-1 polypeptide;~~

~~(ii)~~ (i) a 5'-polynucleotide probe capable of being cleaved by a FEN-1 polypeptide, comprising a 3'-region that is capable of specifically hybridizing under said cleavage conditions to a first portion of the target sequence ~~nucleic acid~~ and a 5'-region located immediately 5' to the 3'-region; and

~~(iii)~~ (ii) a 3'-polynucleotide probe comprising a 5'-region that is capable of specifically hybridizing under said cleavage conditions to a second portion of the target sequence ~~nucleic acid~~ which is located immediately 3' to the first portion and a 3'-region located immediately 3' to the 5'-region, ~~under conditions in which~~ such that the 3'-region of the 5'-probe and the 5'-region of the 3'-probe specifically hybridize immediately contiguously with one another to the first and second portions, respectively, of the ~~same~~ target sequence ~~nucleic acid molecule~~ to form a 5',3'-double flap structure cleavable by a FEN-1 polypeptide; ~~and~~

(b) cleaving the 5',3'-double flap structure with a FEN-1 polypeptide; and

~~(b)~~ (c) detecting the presence or absence of, and/or quantifying the amount of, FEN-1 polypeptide-generated cleavage, thereby detecting the presence of the target sequence ~~nucleic acid~~ in the sample.

23. (Amended) The method of Claim 22 in which the 5'-region of the 5'-probe ~~comprises a 5' flap region that~~ contains ~~a~~ the detectable label.

24. (Amended) The method of Claim 23 in which the 5'-end of the 5'-probe contains ~~a~~ the detectable label.

26. (Amended) The method of Claim 21 in which the FEN-1 polypeptide is ~~a mammalian or a yeast FEN-1 polypeptide~~ encoded by a polynucleotide comprising a sequence selected from the group of sequences consisting of SEQ ID NOS: 29-51.

27. (Amended) The method of Claim 26 in which the FEN-1 polypeptide is ~~a yeast FEN-1 polypeptide, a murine FEN-1 polypeptide or a human FEN-1 polypeptide~~ encoded by a polynucleotide comprising SEQ ID NO:28.

28. (Amended) The method of Claim ~~26~~ 21 in which the FEN-1 polypeptide ~~is a human FEN-1 polypeptide comprising~~ comprises the amino acid sequence shown in SEQ ID NO:1 or a fragment thereof having 5'-flap endonucleolytic cleavage activity.

29. (Amended) The method of Claim ~~26~~ 21 in which the FEN-1 polypeptide ~~is a murine FEN-1 polypeptide comprising~~ comprises the amino acid sequence shown in SEQ ID NO:3 or a fragment thereof having 5'-flap endonucleolytic cleavage activity.

30. (Amended) The method of Claim ~~26~~ 21 in which the FEN-1 polypeptide ~~is a yeast FEN-1 polypeptide comprising~~ comprises the amino acid sequence shown in SEQ ID NO:5 or SEQ ID NO:7 or a fragment thereof having 5'-flap endonucleolytic cleavage activity.

31. (Amended) The method of Claim 21 in which the 3'-region of the 3'-probe ~~comprises a 3' flap region that~~ is 1 to 10 nucleotides in length.

32. (Amended) The method of Claim 21 in which the ~~3' flap region~~ 3'-region of the 3'-probe is 1 nucleotide in length.

33. (Amended) The method of Claim 21 in which the 5'-region of the 5'-probe ~~comprises a 5' flap region that~~ is 1 to 20 nucleotides in length.

53. (Amended) The hybridization complex of Claim 52 in which the 5'-region of the first probe contains ~~a~~ the detectable label.

54. (Amended) The hybridization complex of Claim 53 in which the 5'-end of the first probe contains ~~a~~ the detectable label.

56. (Amended) The hybridization complex of Claim 51 in which the 3'-region of the second probe ~~comprises a 3' flap region that~~ is 1 to 10 nucleotides in length.

57. (Amended) The hybridization complex of Claim 56 in which the ~~3' flap region~~ 3'-region of the second probe is 1 nucleotide in length.

58. (Amended) The hybridization complex of Claim 51 in which the 5'-region of the first probe ~~comprises a 5' flap region that~~ is 1 to 20 nucleotides in length.

59. (Thrice Amended) A kit for use in detecting the presence of a predetermined target nucleic acid sequence in a sample, comprising:

(a) a FEN-1 polypeptide;

(b) a first polynucleotide probe capable of being cleaved by a FEN-1 polypeptide, comprising a 3'-region capable of specifically hybridizing under FEN-1 polypeptide cleavage conditions to a first portion of a the predetermined target sequence ~~nucleic acid of interest~~ and a 5'-region located immediately 5' to the 3'-region; and

(c) a second polynuclcotide probe comprising a 5'-region capable of specifically hybridizing under FEN-1 polypeptide cleavage conditions to a second portion of the target ~~nucleic acid~~ sequence which is located immediately 3' to the first portion and a 3'-region located immediately 3' to the 5'-region,

wherein the 3'-region of the first probe and the 5'-region of the second probe are capable of specifically hybridizing immediately contiguously with one another to the first and second portions, respectively, of the ~~same~~ target ~~nucleic acid molecule~~ sequence to form a 5',3'-double flap structure that is capable of being ~~bound or~~ cleaved by the FEN-1 polypeptide.

62. (Amended) The kit of Claim 59 in which the 3'-region of the second probe ~~comprises a 3' flap region that~~ is 1 to 10 nucleotides in length.

63. (Amended) The kit of Claim 59 in which the ~~3' flap region~~ 3'-region of the second probe is 1 nucleotide in length.

64. (Amended) The kit of Claim 59 in which the 5'-region of the first probe ~~comprises a 5' flap region that~~ is 1 to 20 nucleotides in length.

66. (Amended) The kit of Claim ~~59~~ 65 in which the 5'-region of the first probe ~~comprises a 5' flap region that~~ contains ~~a~~ the detectable label.

67. (Amended) The kit of Claim 66 in which the 5'-end of thc first probe contains ~~a~~ the detectable label.

69. (Amended) The kit of any one of Claim 59-68 in which the FEN-1 polypeptide is ~~a mammalian or a yeast FEN-1 polypeptide~~ encoded by a polynucleotide comprising a sequence selected from the group of sequences consisting of SEQ ID NOS: 29-51.

70. (Amended) The kit of ~~Claim 69~~ any one of Claims 59-68 in which the FEN-1 polypeptide is ~~a yeast FEN-1 polypeptide, a murine FEN-1 polypeptide or a human FEN-1 polypeptide~~ encoded by a polynucleotide comprising SEQ ID NO. 28.

71. (Amended) The kit of ~~Claim 70~~ any one of Claims 59-68 in which the FEN-1 polypeptide ~~is a human FEN-1 polypeptide comprising~~ comprises the amino acid sequence shown in SEQ ID NO:1 or a fragment thereof having 5'-flap endonucleolytic cleavage activity.

72. (Amended) The kit of ~~Claim 70~~ any one of Claims 59-68 in which the FEN-1 polypeptide ~~is a murine FEN-1 polypeptide comprising~~ comprises the amino acid sequence shown in SEQ ID NO:3 or a fragment thereof having 5'-flap endonucleolytic cleavage activity.

73. (Amended) The kit of ~~Claim 70~~ any one of Claims 59-68 in which the FEN-1 polypeptide ~~is a yeast FEN-1 polypeptide comprising~~ comprises the amino acid sequence shown in SEQ ID NO:5 or SEQ ID NO:7 or a fragment thereof having 5'-flap endonucleolytic cleavage activity.